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ABSTRACT

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Effects of various artificial atmospheres, with reduced total pressure and normal O_2 content, are examined. Pure O_2 atmospheres are tested with 148 white rats for 100 days at 198 mm Hg. Effects on reflexes, reaction to stimuli, and physical and cardiac changes are discussed. Author

The development of space science has enhanced the significance of research on the effects of prolonged exposure to an artificial atmosphere. Much theoretical and practical interest has been aroused by investigations to determine the possibility of an organism living long in an atmosphere of pure oxygen at a pressure that eliminates its toxic effect. /1*

Recent extensive discussions by Americans suggest using a single gas, oxygen, in spacecraft living compartments. Schaefer (1964) reports that American physiologists think it desirable to maintain an atmosphere of oxygen alone on craft designed to fly only two weeks. This was carried out in the Mercury and Gemini projects planned for two weeks of flight. In Apollo-type vehicles, designed for longer trips, it was first planned to create an atmosphere of 50 percent O_2 and 50 percent N_2 at a general pressure of 362 mm Hg, but was later changed to oxygen alone due to the need to reduce launch weight (Nonosita, 1964).

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*Numbers given in the margin indicate the pagination in the original foreign text.

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Most authors believe that a "one-gas" atmosphere has several advantages of interest to designers and physiologists. If used, pressure in the cabin could be lowered to one-fourth of the standard atmosphere, thus permitting a marked reduction in the weight of the cabin. It would also make it possible to simplify the air regeneration and control system, reduce the leakage of gas from the cabin to a minimum, and completely eliminate the danger of aeroembolism in the astronauts during decompression. Wherever the need to reduce the launch weight of a vehicle is a major concern, interest in this kind of an atmosphere is understandable. /2

On the other hand, the suggested atmosphere also has some serious disadvantages so that it must be used with great care. The subject as a whole has been very little studied and the implementation of recommendations lacking an adequate scientific basis could be dangerous. We know, for example, that breathing pure oxygen may result in atelectasis, which adversely affects oxygenation of the blood and conduces to the development of focal inflammations in the lungs. Even at a low partial pressure, pure oxygen mildly irritates the upper respiratory tract.

Furthermore, the absence of the inert gas nitrogen in the cabin considerably increases the danger of fire, which could be disastrous to the crew during flight.

It is still far from clear whether a living organism can live and grow in an atmosphere lacking in nitrogen. We still do not know if this gas has any effect on the intimate /3 physiological and biochemical processes of the organism.

Heather (1961) carried out an experimental study on human beings in a pressure chamber with rarefactions corresponding to altitudes of 8400 and 10,200 m. After 14 and 17 days the subjects exhibited symptoms of irritation of the respiratory tract and lung tissue and most lost weight. A similar but more comprehensive investigation was conducted by Wolch, Morgan, et al. (1961) on human beings who remained in a pressure chamber for 30 days at an altitude of 5500 m and for 17 days at an altitude of 10,200 m. The purpose was to study the effects of a rarefied atmosphere in the absence of an inert gas and the influence of prolonged inactivity and isolation. The authors noted a drop in diastolic pressure, lengthening of the time required for the pulse to return to normal after an orthostatic test, decrease in the vital capacity of the lungs, and symptoms of irritation of the respiratory tract and mucosa. The subjects lost 2.8-3.6 kg of weight after 30 days, 2 kg after 17 days. The water content of the tissues decreased, but the fat content rose.

The experiments of McHattie and Rahn (1960) and of Berry and Smith (1962) showed that mice can survive and produce normal offspring in a single-gas atmosphere at a general pressure of 197 mm Hg. They concluded that the lack of nitrogen in the ∠4
atmosphere has no effect on the course of the major life processes. However, judging by Allen's experiments (1962), it would be premature to categorically deny that nitrogen plays a biological role in the animal organism. He found that the vascular system of chick

embryos does not develop in an exclusively oxygen medium at a pressure of 150 mm Hg because of the lack of nitrogen. The need for further study of the subject is obvious.

Soviet experts are guided by the principle of maximum caution in dealing with the problems involved in selecting an atmosphere for spacecraft. The choice has to be scientifically grounded. It must meet reasonable standards of comfort, be harmless, and permit continuous regeneration by reliable apparatus. However, it would be a mistake to think that an atmosphere could be chosen for spacecraft that would be suitable for all conditions.

The use of an atmosphere in the cabins of the Vostok and Voskhod with parameters similar to that on earth has been largely justified and there seems to be no serious objections to using it on future brief orbital flights. Nevertheless, we must continue to study variations of an artificial atmosphere in order to broaden our technical and biological capabilities for building life-support systems to protect man in space. /5

The purpose of this investigation was to make a comprehensive study of the effects of a 100 day exposure to an atmosphere of pure oxygen at a general minimum ambient pressure, with the gas supplied to animals in adequate quantities.

Method. Experiments were performed on white rats in a pressure chamber equipped with a life-support system based on the following parameters: O_2 - 95%; CO_2 - 0.3-0.5%; temperature - 20-23° C; relative humidity - 50-70%. Water and food was supplied to the animals by means of a semiautomatic device. The feed consisted of 2/3 wheat groats and 1/3 oats. The animals were given bread, meat, and vitamins four times a month.

There was a device to remove harmful impurities from the air of the chamber so that the amount of ammonia, carbon monoxide, hydrocarbons, etc. did not exceed the maximum permissible concentrations. Each cage had a drip pan filled with silica gel to absorb the urine. The silica gel was changed regularly. The arrangement of the chamber enabled the personnel to enter and leave without interfering with the atmospheric conditions therein. To prevent aeroembolism, decompression of the chamber was gradually lowered from 760 to 198 mm Hg.

There were 148 experimental animals and 55 controls kept on the same food and water regime. The behavior and general condition of the animals, higher nervous activity, weight dynamics, some aspects of water-salt metabolism, biochemical indices of the blood, changes in formed elements of the peripheral blood, and morphological changes in the viscera were kept under observation.

The results showed that there were no changes in the animals' behavior and condition that endangered their lives or impaired the functioning of the most important body systems. Food excitability was adequate throughout the experiment as was the reactivity to the surrounding laboratory conditions. /6

Conditioned reflexes. An automatic apparatus was designed for this purpose. The electrical circuit and general view are shown in fig. 1.

A chain of motor reflexes was formed by the method described by Voronin and Napalkov (1959). A stereotype composed of 18 positive chain stimuli and 6 conditioned inhibitory stimuli was used in each experiment. This method makes it possible to investigate the fine processes of analysis and synthesis of complex stimuli acting on the organism in a definite sequence. Consequently, a physiological experiment comes very close to duplicating the natural interactions of the organism with the external environment whereby the leading role in the phenomena of adaptation is played not by simple conditioned signals but by the influence of complexes and chains of stimuli.

During the first few days of exposure the rats displayed slightly more vigorous orienting-search activity than usual.and had more reactions between signals along with increased general motor activity. Most presentations of the chain stimulus /7 elicited a distinct chain motor reflex. Loss of reflexes was exceptional and only during the first month of the experiment. This clearly indicated that under the conditions of the exclusively oxygen atmosphere under study, analysis and synthesis of the chain of previously formed food-grasping movements remained essentially unimpaired.

The situation was different with respect to the reaction of conditioned disinhibition formed from a chain of positive signals. It was found that if an obstacle was in the way of executing the positive food-grasping reflex and the animal was taught to get around it at an additional signal, then the animal quickly gained the capacity to perform this act under normal circumstances. Inadequate reactions were rare (fig. 2).

The animals reacted inadequately to inclusion of the conditioned inhibitory stimulus. The decrease in adequate reactions was particularly pronounced throughout the first and part of the second months of the experiment. Sometimes the animals failed to perceive the signal of the additional component of the conditioned stimulus and completed movements caused by the stereotype of the positive chain. In doing so they received no food and returned to the starting place where they waited for the next signal. During the second half of the experiment the animals' reactions to the conditioned stimuli gradually returned to normal and the data obtained in the /8
period of the aftereffect more or less coincided with the results of the control period. We regard the inadequate reactions to inclusion of the signal of conditioned inhibition as the consequence of a weakening of the process of internal active inhibition.

Change in weight. During the first half of the experiment (50 days), the experimental animals lost as much as 25% of their original weight. But from the 55th day on they began to gain weight and by the end of the experiment the increase was more marked than in the control animals. At this time the weight balance of the experimental rats (72 g) exceeded that of the control (56 g) by 16 g.

There are grounds for believing that the negative weight balance may be caused by an increase in water loss due to low ambient pressure. In experiments on animals in a pressure chamber (altitudes of 5000-8000 m), Kuznetsov (1955), Van Lier (1942), and Swann and Collings (1943) observed increased diuresis, intensified excretion of sodium chloride with urine, and weight loss. These phenomena, according to the authors, were caused by acute hypoxia and resultant hyperventilation of the lungs, which greatly intensifies the loss of water through the respiratory tract.

In our investigation, the oxygen supply of the animals was adequate and the loss of water was due solely to the independent effect of low ambient pressure. There is no direct, sound evidence in the literature that low barometric pressure intensifies the loss of water by the organism. We know only that 19
evaporation increases due to a reduction in the number of collisions of the evaporating molecules with the molecules of gas whose concentration is reduced by a lowering of pressure. This was shown by the direct measurementsof water evaporation under the conditions of normal and low barometric pressure that were made by A. I. Shaposhnikov and B. S. Perepletchikova during this investigation.

It is evident from Table 1 that the amount of water that evaporates from level surfaces at low pressure is almost twice that at normal pressure.

Table 1

Parameters	760 mm Hg	198 mm Hg
Temperature	20-23°C	20-25°C
Humidity	45-65%	42-75%
Amount of water evaporated, g	1125	2150
Rate of evaporation $g/cm^2/hour$	2.5	4.4

If the loss of weight under these conditions is caused by increased emission of water, it naturally would affect the water content of the tissues, chiefly skin, muscle and liver, which are usually regarded as a depot of body fluids. An investigation showed that the water content of the skin and muscles decreased (as determined by the gravimetric method) at the same time that the animals were losing weight. These changes were pronounced in the skin tissue in which the water content dropped by almost one-half during the /10
15 days of the experiment. The drop in water content of the liver, muscles, and blood was insignificant.

These findings seem to confirm the assumption that the loss of weight by animals and human beings exposed to a rarefied atmosphere is attributable to intensified emission of water from the skin and lungs.

Since the emission of water by evaporation is a physical phenomenon, it is reasonable to expect it to happen as long as the rarefied atmosphere prevails. However, as mentioned above, the animals lost weight only during the first half of the experiment. During the second half they kept on gaining and by the end of the experiment they weighed more than the control animals. Clearly, the changes in water metabolism cannot account for the marked fluctuations in weight observed under the conditions of a rarefied atmosphere. They are undoubtedly also related to changes in the metabolic processes.

The phenomenon of weight loss and gain is of considerable scientific interest in still another respect, for it implies the presence of an active factor whose physiological role has hitherto been denied in the literature. The facts show that low atmospheric pressure (with normal pO_2) by itself has some effect on the body and that the body gradually adapts to the new 11
medium. The length of time required for adaptation is apparently determined by the degree of rarefaction of the atmosphere. According to our provisional data, the time required for adaptation to an atmosphere with normal pO_2 and low general ambient pressure up to 308 or 198 mm Hg was 30-35 or 55-60 days, respectively (A. G. Kuznetsov, N. A. Agadzhanyan, A. G. Dianov, and S. G. Zharov, 1964). It is interesting to note that the cycle of changes in the peripheral blood was completed at about the same time. There was an increase in the hemoglobin concentration (120%), number of erythrocytes (134%) and reticulocytes (160%); this level was maintained for 43 days. By the 58th day the blood indices returned to normal, remaining unchanged thereafter until the end of the experiment (N. I. Yezepchuk).

Biological Role of Nitrogen. Rats kept in an atmosphere without nitrogen survived for 100 days and produced normal offspring (at a pressure of 198 mm Hg). It is interesting to note that the period of pregnancy lengthened by 5-7 days. The limited number of observations naturally do not rule out the element of chance here. Nevertheless, the partial coincidence of our data with those of Allen (1962) on the arrested development of the vascular system of chick embryos under the same conditions suggests that atmospheric nitrogen plays a major role in the development of vital functions.

A study was also made of the effect of a nitrogen-less /12 atmosphere on the development of atelectases. V. A. Vinogradov found indistinct atelectases in the perihilar zone. These were particularly marked in the animals kept in a pure oxygen atmosphere the first two days. No atelectases were observed in the animals examined later, indicating that the collapse of lung tissue was reversible. No signs of toxicity or irritation of lung tissue were noted. Throughout the experiment blood pO_2 remained high; pCO_2 was somewhat low (Ye. A. Kovalenko).

Change in Microflora. N. N. Sitnikova observed that the quantity of microflora in the chamber increased five-fold during the experiment and the microbial landscape was featured by a predominance of forms more resistant to the external environment - spore-bearing, aerobic, fungus. We see here a case of direct organism-environment interaction.

Conclusion

Prolonged exposure (100 days) of animals to an atmosphere consisting solely of oxygen at a general pressure of 198 mm Hg does not endanger life or impair general health. This indicates that such an atmosphere can be used for practical purposes. We also showed that such exposure at low general pressure and with normal oxygen content of the atmosphere gives /13
rise to distinct changes in several important physiological functions. The phenomena gradually level out and within 50-60 days the functions return to normal, an indication that adaptation has been effective. This proves that low atmospheric pressure has independent biological significance, which should be kept in mind when studying the problem of making spacecraft habitable under the conditions of a rarefied atmosphere.

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Bibliography

1. Voronin, L. G. and Napalkov, A. V. "Methods of Forming Complex Sets of Motor Conditioned Reflexes," Zh. VND (Journal of Higher Nervous Activity), Vol. 9, No. 5, 1959.

2. Kuznetsov, A. G. "Effect of Hypoxemia on Kidney Function," in the collection: Funktsii organizma v usloviyakh izmenennoy gazovoy sredy (Body Functions in an Altered Gas Medium), Izd-vo AN SSSR, Vol. 1, pp. 172-199, 1955.

3. Kuznetsov, A. G., Agadzhanyan, N. A., Dianov, A. G., and Zharov, S. G. Trudy XV Mezhdunarodnogo astronavticheskogo kongressa (Proceedings of the Fifteenth International Astronautical Congress), Warsaw, September, 1964.

4. Allen, S. The Physiol., Vol. 5, p. 98, 1962.

5. Berry, L. and Smith, D. Amer. Jour. Physiol., Vol. 203 (1), 1962, p. 155.

6. Van Lier, E. Anoxia, Chicago, 1942.

7. Wolch, Morgan, et al. J. Aerospace Medicine, Vol. 32, No. 7, p. 583, 1961.

8. McHattie, L. and Rahn, H. Proc. Soc. Exp. Biol. and Medicine, Vol. 3, pp. 69-79, 1960.

9. Nonosita, R. Space Aeronautics, Vol. 3, pp. 69-69, 1964.

10. Swann and Collings. Aviation Med., Vol. 3, pp. 114-118, 1943.

11. D. Heather. Missiles and Rockets, Vol. 9, No. 4, p. 44, 1961.

12. K. Schaefer. Bioastronautics, pp. 76-110, 1964.